IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application. No.	:	10/723,933
Inventors/Applicants	:	Kenneth James, et al.
Filed	:	November 26, 2003
TC/A.U.	:	1642
Confirmation No.	:	9468
Examiner	:	UNKNOWN
Atty. Docket No.	:	014811-205.108
Customer No.	:	24,239

Title: NATRIUTETIC COMPOUNDS, CONJUGATES, AND USES THEREOF

PETITON FOR REVIVAL OF AN APPLICATION FOR PATENT ABANDONED UNAVOIDABLY UNDER 37 CFR 1.137(a) IN U.S. PATENT APPLICATION NO. 10/723,933

ATTENTION: OFFICE OF PETITIONS
Mail Stop: Petition
Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

Sir:

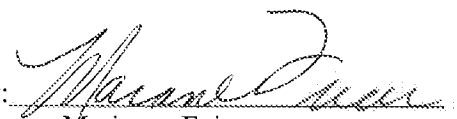
Attached please find an attached petition and the fee of $500.00 is being electronically transferred. If any additional fee is found due, the Commission is authorized to charge such fee to Deposit Account No. 13-4365 of Moore & Van Allen, PLLC.

If any issues remain outstanding, the applicants request the undersigned attorney be contacted at 919-286-8089.

Respectfully submitted,

MOORE & VAN ALLEN PLLC

Date: 8/8/07

By: 

Marianne Fuierer
Attorney for Applicants
Registration No. 39983

Atty. Docket No. 014811-205.108

Moore & Van Allen PLLC
430 Davis Drive, Suite 500
Morrisville, NC 27560-6832

PTO/SB/61 (10-05)
Approved for use through 07/31/2006. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

PETITION FOR REVIVAL OF AN APPLICATION FOR PATENT ABANDONED UNAVOIDABLY UNDER 37 CFR 1.137(a)	Docket Number (Optional) 014811-205.108

First Named Inventor: Kenneth James
Art Unit: 1642
Application Number: 10/723,933
Examiner: UNKNOWN
Filed: November 26, 2003

Title: NATRIUTETIC COMPOUNDS, CONJUGATES, AND USES THEREOF

Attention: Office of Petitions
Mail Stop Petition
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

NOTE: If information or assistance is needed in completing this form, please contact Petitions Information at (571) 272-3282.

The above-identified application became abandoned for failure to file a timely and proper reply to a notice or action by the United Sates Patent and Trademark Office. The date of abandonment is the day after the expiration date of the period set for reply in the Office notice or action plus any extensions of time actually obtained.

APPLICANT HEREBY PETITIONS FOR REVIVAL OF THIS APPLICATION.

NOTE: A grantable petition requires the following items:
(1) Petition fee.
(2) Reply and/or issue fee.
(3) Terminal disclaimer with disclaimer fee-required for all utility and plant applications filed before June 8, 1995, and for all design applications; and
(4) Adequate showing of the cause of unavoidable delay.

1. Petition fee

☐ Small entity – fee $_____ (37 CFR 1.17(l)). Applicant claims small entity status. See 37 CFR 1.27.

☒ Other than small entity – fee $ $500.00 (37 CFR 1.17(l)).

2. Reply and/or fee

A The reply and/or fee to the above-noted Office action in the form of _____ (identify the type of reply):

☐ has been filed previously on _____ .

☒ is enclosed herewith.

B The issue fee of $ _____

☐ has been filed previously on _____ .

☐ is enclosed herewith.

PETITION FOR REVIVAL OF AN APPLICATION FOR PATENT ABANDONED UNAVOIDABLY UNDER 37 CFR 1.137(a)

3. Terminal disclaimer with disclaimer fee

☐ Since this utility/plant application was filed on or after June 8, 1995, no terminal disclaimer is required.

☐ A terminal disclaimer (and disclaimer fee (37 CFR 1.20(d)) of $ _____ for a small entity or $ _____ for other than a small entity) disclaiming the required period of time is enclosed herewith (see PTO/SB/63).

4. An adequate showing of the cause of the delay, and that the entire delay in filing the required reply from the due date for the reply until the filing of a grantable petition under 37 CFR 1.137(a) was unavoidable, is enclosed.

WARNING:

Petitioner/applicant is cautioned to avoid submitting personal information in documents filed in a patent application that may contribute to identity theft. Personal information such as social security numbers, bank account numbers, or credit card numbers (other than a check or credit card authorization form PTO-2038 submitted for payment purposes) is never required by the USPTO to support a petition or an application. If this type of personal information is included in documents submitted to the USPTO, petitioners/applicants should consider redacting such personal information from the documents before submitting them to the USPTO. Petitioner/applicant is advised that the record of a patent application is available to the public after publication of the application (unless a non-publication request in compliance with 37 CFR 1.213(a) is made in the application) or issuance of a patent. Furthermore, the record from an abandoned application may also be available to the public if the application is referenced in a published application or an issued patent (see 37 CFR 1.14). Checks and credit card authorization forms PTO-2038 submitted for payment purposes are not retained in the application file and therefore are not publicly available.

_____	August 8, 2007
Signature	Date
Marianne Fuierer	39,983
Typed or printed name	Registration Number, if applicable
P. O. Box 13706	919-286-8000
Address	Telephone Number
Research Triangle Park, NC 27709	
Address	

Enclosure
- [X] Fee Payment
- [ ] Reply
- [ ] Terminal Disclaimer Form
- [X] Additional sheets containing statements establishing unavoidable delay
- [ ] _____

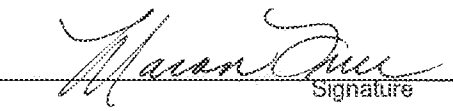
CERTIFICATE OF MAILING OR TRANSMISSION (37 CFR 1.8(a))

I hereby certify that this correspondence is being:

☐ deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to **Mail Stop Petition**, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

☒ Filed by electronic transfer.

August 8, 2007
Date


Signature

Marianne Fuierer
Typed or printed name of person signing certificate

PTO/SB/61 (10-05)
Approved for use through 07/31/2006. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

PETITION FOR REVIVAL OF AN APPLICATION FOR PATENT ABANDONED UNAVOIDABLY UNDER 37 CFR 1.137(a)

NOTE: The following showing of the cause of unavoidable delay must be signed by all applicants or by any other party who is presenting statements concerning the cause of delay.

Signature

August 8, 2007
Date

Marianne Fuierer
Typed or printed name

39,983
Registration Number, if applicable

(In the space provided below, please explain in detail the reasons for the delay in filing a proper reply.)

Applicants received a Notice of Abandonment (Appendix A) because according to the Office of Initial Patent Examination, applicants did not file a response to the November 16, 2006 Office Action. Clearly it is evident, by the attached document, that applicants did file a response. Applicant thought that receiving an Auto Reply from the PTO was sufficient proof to show that all requirements were of filing a response were met.

The issued Notice to Comply provided instructions why the application did not comply with the sequence rules. Specifically, some of the claims did not include sequence identifier. Notably, the Sequence Rule Compliance Review Item did not state that there was anything physically wrong with sequence listings or disk that was submitted on May 19, 2004 but instead stated that some of the claims did not include sequence identifiers (Appendix B). As such, there was nothing wrong with the previous submission of the sequence listing, computer readable disk or Statement of Identity, but instead claims needed to be amended to recite sequence identifiers that were included in the previously submitted sequence listing. Applicants amended the claims as requested and submitted same (Appendix C). Further, the previous submitted sequence listing and disk met all legal requirements.

Further, since applicants met all the requirements for filing the response, and the abandonment was due to a mistake at the USPTO, applicants should not be charge for this petition.

As such, Applicants request that this Petition for Revival of the US Abandoned Unavoidably under 37 CFR 1.137(a) be granted without cost to applicants.

Appendix A

UNITED STATES PATENT AND TRADEMARK OFFICE

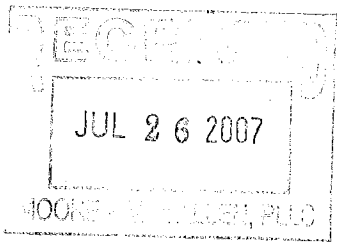
UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING OR 371(C) DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO./TITLE
10/723,933	11/26/2003	Kenneth D. James	014811-205.108

CONFIRMATION NO. 9468

ABANDONMENT/TERMINATION LETTER

24239
MOORE & VAN ALLEN PLLC
P.O. BOX 13706
Research Triangle Park, NC 27709



Date Mailed: 07/24/2007

NOTICE OF ABANDONMENT UNDER 37 CFR 1.53 (f) OR (g)

The above-identified application is abandoned for failure to timely or properly reply to the Notice to File Missing Parts (Notice) mailed on 11/16/2006.

- No reply was received.

If a complete reply to the notice was previously filed by applicant within the time period set forth in the notice, applicant may request for reconsideration of the holding of abandonment within 2 months from the mailing of this notice of abandonment by filing a petition to withdraw the holding of abandonment under 37 CFR 1.181(a). No petition fee is required. The petition must be accompanied by a true copy of the originally filed reply and the item (s) identified in one of the following:

1. A properly itemized date-stamped postcard receipt (see MPEP § 503);

2. If the originally filed reply included a certificate of mailing or transmission in compliance with 37 CFR 1.8(a), a copy of the certificate of mailing or transmission and a statement in compliance with 37 CFR 1.8(b) (see MPEP § 512); or

3. If the reply was filed via "Express Mail," a submission satisfying the requirements of 37 CFR 1.10(e) including, for example, a copy of the "Express Mail" mailing label showing the "date-in" (see MPEP § 513).

Any petition to withdraw the holding of abandonment should be directed to OIPE.

If applicant did not previously file a complete reply within the time period set forth in the notice, applicant may file a petition to revive the application under 37 CFR 1.137.

Under 37 CFR 1.137(a), a petition requesting the application be revived on the grounds of **UNAVOIDABLE DELAY** must be filed promptly after the applicant becomes aware of the abandonment and such petition must be accompanied by: (1) an adequate showing of the cause of unavoidable delay; (2) the required reply to the above-identified Notice; (3) the petition fee set forth in 37 CFR 1.17(l); and (4) a terminal disclaimer if required by 37 CFR 1.137(d). See MPEP § 711.03(c) and Form PTO/SB/61.

Under 37 CFR 1.137(b), a petition requesting the application be revived on the grounds of **UNINTENTIONAL DELAY** must be filed promptly after applicant becomes aware of the abandonment and such petition must be accompanied by: (1) a statement that the entire delay was unintentional; (2) the required reply to the above-identified Notice; (3) the petition fee set forth in 37 CFR 1.17(m); and (4) a terminal disclaimer if required by 37

CFR 1.137(d). See MPEP § 711.03(c) and Form PTO/SB/64.

Any questions concerning petitions to revive should be directed to the "Office of Petitions" at (571) 272-3282.

A copy of this notice MUST be returned with the reply.

Office of Initial Patent Examination (571) 272-4000, or 1-800-PTO-9199
PART 1 - ATTORNEY/APPLICANT COPY

Appendix B

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NUMBER	FILING OR 371 (c) DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NUMBER
10/723,933	11/26/2003	Kenneth D. James	014811-205.108

CONFIRMATION NO. 9468

FORMALITIES LETTER

24239
MOORE & VAN ALLEN PLLC
P.O. BOX 13706
Research Triangle Park, NC 27709

Date Mailed: 11/16/2006

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Filing Date Granted

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR §§ 1.821-1.825. The application must be in sequence compliance before examination on the merits.

APPLICANT IS GIVEN ONE MONTH FROM THE DATE OF THIS LETTER WITHIN WHICH TO COMPLY WITH THE SEQUENCE RULES, 37 CFR §§ 1.821-1.825. Failure to comply with these requirements will result in ABANDONMENT of the application under 37 CFR § 1.821(g). Extension of time may be obtained by filing a petition accompanied by the extension fee under the provisions of 37 CFR § 1.136. In no case may an applicant extend the period for response beyond the six-month statutory period. Direct the response to: Mail Stop Missing Parts, Commissioner for Patents, P.O. Box 1450, Alexandria VA 22313-1450.

See the attachment.

Applicant Must Provide as part of the response:

- An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".
- An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.
- A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 CFR 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

To Download Patentin Software, visit http://www.uspto.gov/web/patents/software.htm
For questions regarding compliance to these requirements, please contact:

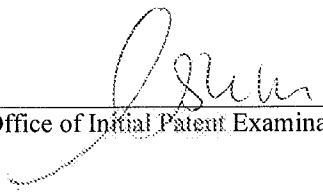
- **For Rules Interpretation, call (571) 272-0951**
- **For Patentin Software Program Help, call Patent EBC at 1-866-217-9197 or directly at 703-305-3028 / 703-308-6845 between the hours of 6 a.m. and 12 midnight, Monday through Friday, EST.**
- **Send e-mail correspondence for Patentin Software Program Help @ ebc@uspto.gov**

Replies should be mailed to: Mail Stop Missing Parts
Commissioner for Patents
P.O. Box 1450
Alexandria VA 22313-1450

Registered users of EFS-Web may alternatively submit their reply to this notice via EFS-Web.
https://sportal.uspto.gov/authenticate/AuthenticateUserLocalEPF.html

For more information about EFS-Web please call the USPTO Electronic Business Center at **1-866-217-9197** or visit our website at http://www.uspto.gov/ebc.

If you are not using EFS-Web to submit your reply, you must include a copy of this notice.



Office of Initial Patent Examination (571) 272-4000, or 1-800-PTO-9199, or 1-800-972-6382
PART 2 - COPY TO BE RETURNED WITH RESPONSE

OIPE ROUTING SHEET

APPLICATION

10/723,933

IFW DocCode- SEQREQ

Index using Current Date

TO BE DELIVERED TO:

Tech Center Scanning

Sequence Rule Compliance Review Item

	CRF, paper copy of sequence listing, and statement that both are same missing
	CRF contains error(s) according to STIC Report
	CRF damaged or unreadable according to STIC Report
	CRF transferred from prior application is not compliant
X	OTHER

Place an "X" in the appropriate box

Cecilia J. Tsang
Supervisory Patent Examiner
Technology Center 1600

Appendix C

Acknowledgement Receipt

The USPTO has received your submission at **16:07:45** Eastern Time on **15-FEB-2007** .

$ **450** fee paid by e-Filer via *RAM* with Confirmation Number: 378.

eFiled Application Information

EFS ID	1519613
Application Number	10723933
Confirmation Number	9468
Title	Natriuretic compounds, conjugates, and uses thereof
First Named Inventor	Kenneth D. James
Customer Number or Correspondence Address	24239
Filed By	Marianne Fuierer
Attorney Docket Number	014811-205.108
Filing Date	26-NOV-2003
Receipt Date	15-FEB-2007
Application Type	Utility

Application Details

Submitted Files	Page Count	Document Description	File Size	Warnings
Response_to_Notice_to_Comply.pdf	32		1120855 bytes	◆ PASS

Document Description	Page Start	Page End
Amendment Copy Claims/Response to Suggested Claims	1	31
Applicant Arguments/Remarks Made in an Amendment	32	32

fee-info.pdf	2	Fee Worksheet (PTO-06)	8140 bytes	◆ PASS

This Acknowledgement Receipt evidences receipt on the noted date by the USPTO of the indicated documents, characterized by the applicant, and including page counts, where applicable. It serves as evidence of receipt similar to a Post Card, as described in MPEP 503.

New Applications Under 35 U.S.C. 111

If a new application is being filed and the application includes the necessary components for a filing date (see 37 CFR 1.53(b)-(d) and MPEP 506), a Filing Receipt (37 CFR 1.54) will be issued in due course and the date shown on this Acknowledgement Receipt will establish the filing date of the application.

National Stage of an International Application under 35 U.S.C. 371

If a timely submission to enter the national stage of an international application is compliant with the conditions of 35 U.S.C. 371 and other applicable requirements a Form PCT/DO/EO/903 indicating acceptance of the application as a national stage submission under 35 U.S.C. 371 will be issued in addition to the Filing Receipt, in due course.

If you need help:

- *Call the Patent Electronic Business Center at (866) 217-9197 (toll free) or e-mail EBC@uspto.gov for specific questions about Patent e-Filing.*
- *Send general questions about USPTO programs to the USPTO Contact Center (UCC) .*
- *If you experience technical difficulties or problems with this application, please report them via e-mail to Electronic Business Support or call 1 800-786-9199.*

Electronic Patent Application Fee Transmittal

Application Number:	10723933
Filing Date:	26-Nov-2003
Title of Invention:	Natriuretic compounds, conjugates, and uses thereof
First Named Inventor/Applicant Name:	Kenneth D. James
Filer:	Marianne Fuierer
Attorney Docket Number:	014811-205.108

Filed as Large Entity

Utility Filing Fees

Description	Fee Code	Quantity	Amount	Sub-Total in USD($)
Basic Filing:				
Pages:				
Claims:				
Miscellaneous-Filing:				
Petition:				
Patent-Appeals-and-Interference:				
Post-Allowance-and-Post-Issuance:				
Extension-of-Time:				
Extension - 2 months with $0 paid	1252	1	450	450

Description	Fee Code	Qua. .y	Amount	Sub-Total in USD($)
Miscellaneous:				
			Total in USD ($)	450

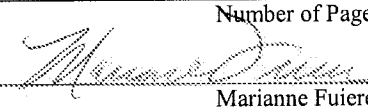
IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re United States Patent Application of:		**Docket No.:**	**014811-205.108**
Applicant:	**Kenneth D. James, et al.**	**Examiner:**	**NA**
Application No.:	**10/723,933**	**Confirmation No.:**	**9468**
Date Filed:	**November 26, 2003**	**Art Unit:**	**1642**
Title:	**NATRIURETIC COMPOUNDS, CONJUGATES, AND USES THEREOF**	**Customer No.:**	**24239**

ELECTRONIC TRANSMISSION CERTIFICATE

I hereby certify that this document is being filed in the United States Patent and Trademark Office, via electronic transmission, Commissioner for Patents, PO Box 1450, Alexandria, VA 22313-1450, to United States Patent and Trademark Office

34
Number of Pages



Marianne Fuierer

February 15, 2006
Date

RESPONSE TO NOVEMBER 16, 2006 NOTICE TO COMPLY; AND PETITION FOR A TWO MONTH EXTENSION UNDER 37 C.F.R. §1.136 IN U.S. PATENT APPLICATION NO. 10/723,933

Commission for Patents
P. O. Box 1450
Alexandria, VA 22313-1450

Sir:

In response to the November 16, 2006 Notice to comply, please amend the application as follows:

In the Claims

1. (Original) A natriuretic compound conjugate comprising:

   (a) a biologically active natriuretic compound comprising:

      (i) a natriuretic molecule NPR-A binding site; and

      (ii) at least one modifying moiety conjugation site; and

   (b) at least one modifying moiety attached to said modifying moiety conjugation site;

   wherein said natriuretic compound conjugate exhibits one or more advantages selected from the group consisting of increased resistance to enzymatic degradation relative to a corresponding unconjugated natriuretic compound, increased circulating half life, increased bioavailability, and prolonged duration of effect.

2. (Original) The natriuretic compound conjugate of claim 1 further defined as retaining a therapeutically significant percentage of cGMP stimulating activity relative to the corresponding unconjugated natriuretic compound.

3. (Original) The natriuretic compound conjugate of claim 1 further defined as retaining at least 30% of the cGMP stimulating activity of the corresponding unconjugated natriuretic compound.

4. (Original) The natriuretic compound conjugate of claim 1 further defined as retaining at least 50% of the cGMP stimulating activity of the corresponding unconjugated natriuretic compound.

5. (Currently amended) The natriuretic compound conjugate of claim 1 wherein the natriuretic compound is hBNP. ~~further defined as retaining at least 70% of the cGMP stimulating activity of the corresponding unconjugated natriuretic compound~~.

6. (Original) The natriuretic compound conjugate of claim 1 further defined as retaining at least 90% of the cGMP stimulating activity of the corresponding unconjugated natriuretic compound.

7. (Original) The natriuretic compound conjugate of claim 1 further defined as more hydrophilic than a corresponding unconjugated natriuretic compound.

8. (Original) The natriuretic compound conjugate of claim 1 further defined as more amphiphilic than a corresponding unconjugated natriuretic compound.

9. (Original) The natriuretic compound conjugate of claim 1 further defined as more lipophilic than a corresponding unconjugated natriuretic compound.

10. (Original) The natriuretic compound conjugate of claim 9 wherein the modifying moiety does not consist of an alkyl moiety.

11. (Original) The natriuretic compound conjugate of claim 1 further defined as more resistant to protease degradation than a corresponding unconjugated natriuretic compound.

12. (Previously presented) The natriuretic compound conjugate of claim 1 wherein the natriuretic compound comprises a sequence:

$A^1PX^1MVQGSGCFGRX^2MDRISSSSGLGCX^3VLR$ (SEQ ID NO. 116).

wherein

A^1 is an amino acid or series of amino acids native to a natriuretic peptide,

X^1, X^2 and X^3 are independently selected from the group consisting of Lys, Arg and Gly, and at least one of X^1, X^2 and X^3 is a Lys.

13. (Original) The natriuretic compound conjugate of claim 1 wherein the natriuretic compound comprises a peptide or a biologically active peptide segment of brain natriuretic peptide, atrial natriuretic peptide, C-type natriuretic peptide, or dendroaspis natriuretic peptide.

14. (Previously presented) The natriuretic compound conjugate of claim 1 wherein the natriuretic compound comprises:

(a) an amino acid sequence

X^1–$C^1FGRX^2MDRISSSSGLGC^2$–X^3 (SEQ ID NO: 117)

wherein

X^1 is optionally present and when present is an amino acid sequence having from 1–10 amino acids;

X^2 is Gly, Arg, or Lys; and

X^3 is optionally present and when present is an amino acid sequence having from 1–10 amino acids.

(b) a disulfide bond between C^1 and C^2 to form a loop.

15. (Original) The natriuretic compound conjugate of claim 14 wherein X^1 is Arg or Gly.

16. (Previously presented) The natriuretic compound conjugate of claim 14 wherein X^1 is selected from the group consisting of:

(a) Lys;

(b) Gly;

(c) Arg;

(d) SG-, GSG-, QGSG- (SEQ ID NO. 118), VQGSG- (SEQ ID NO. 119), MVQGSG- (SEQ ID NO. 120), PKMVQGSG- (SEQ ID NO. 121), and SPKMVQGSG- (SEQ ID NO. 122);

(e) hBNP segments of (d) comprising a substitution selected from the group consisting of Lys-to-Gly and Lys-to-Arg;

(f) hBNP segments of (d) comprising a substitution selected from the group consisting of Gly-to-Lys and Arg-to-Lys;

(g) hBNP segments of (d) comprising an inserted Lys;

(h) N-terminal tails and C-terminal segments of N-terminal tails of natriuretic peptides;

(i) N-terminal tails and C-terminal segments of (h) comprising a substitution selected from the group consisting of Lys-to-Gly and Lys-to-Arg;

(j) N-terminal tails and C-terminal segments of (h) comprising a substitution selected from the group consisting of Gly-to-Lys and Arg-to-Lys;

(k) N-terminal tails and C-terminal segments of (h) comprising an inserted Lys.

17. (Previously presented) The natriuretic compound conjugate of claim 14 wherein X^3 is selected from the group consisting of:

(a) Lys;

(b) Gly;

(c) Arg;

(d) hBNP segments KV, KVL, KVLR (SEQ ID NO. 107), KVLRR (SEQ ID NO. 106), and KVLRRH (SEQ ID NO. 105); and

(e) hBNP segments of (d) comprising a substitution selected from the group consisting of Lys-to-Gly and Lys-to-Arg;

(f) hBNP segments of (d) comprising a substitution selected from the group consisting of Gly-to-Lys and Arg-to-Lys;

(g) hBNP segments of (d) comprising an inserted Lys;

(h) C-terminal tails and N-terminal segments of C-terminal tails of natriuretic peptides;

(i) C-terminal tails and N-terminal segments of C-terminal tails of (h) comprising a substitution selected from the group consisting of Lys-to-Gly and Lys-to-Arg;

(j) C-terminal tails and N-terminal segments of C-terminal tails of (h) comprising a substitution selected from the group consisting of Gly-to-Lys and Arg-to-Lys;

(k) C-terminal tails and N-terminal segments of C-terminal tails of (h) comprising an inserted Lys.

18. (Previously presented) The natriuretic compound conjugate of claim 14 wherein the natriuretic compound comprises a sequence selected from the group consisting of:

(a) SPKMVQGSGCFGRKMDRISSSSGLGCKVL (SEQ ID NO. 123);

(b) SPKMVQGSGCFGRKMDRISSSSGLGC (SEQ ID NO. 124); and

(c) segments (a) or (b) comprising a substitution selected from the group consisting of Lys-to-Gly and Lys-to-Arg .

19. (Original) The natriuretic compound conjugate of claim 14 wherein X^1 comprises a 1-9 amino acid residue sequence from the N-terminus of hBNP.

20. (Previously presented) The natriuretic compound conjugate of claim 14 wherein X^1 comprises $SPX^3MVQGSG$ (SEQ ID NO: 125), and wherein X^2 comprises a modifying moiety conjugation site.

21. (Original) The natriuretic compound conjugate of claim 14 wherein X^3 comprises a 1-6 amino acid residue sequence from the C-terminus of hBNP.

22. (Previously presented) The natriuretic compound conjugate of claim 14 wherein X^3 comprises KVLRRH (SEQ. ID. NO: 105), KVLRR (SEQ ID NO. 106), KVLR (SEQ ID NO. 107), KVL, KV or K.

23. (Previously presented) The natriuretic compound conjugate of claim 1 wherein the natriuretic compound comprises a native hBNP sequence (SEQ ID NO. 73) having one or more mutations selected from the group consisting of Lys3Arg, Lys14Arg, Arg30Lys, Lys27Arg, and Arg31Lys.

24. (Previously presented) The natriuretic compound conjugate of claim 1 wherein the natriuretic compound comprises a native hBNP sequence (SEQ ID NO. 73), having one or more insertions or deletions.

25. (Previously presented) The natriuretic compound conjugate of claim 1 wherein the natriuretic compound comprises a native hBNP amino acid sequence (SEQ ID NO. 73) and a N-terminal or C-terminal Lys.

26. (Original) The natriuretic compound conjugate of claim 1 further defined as:

(a) comprising a multipeptide comprising two or more amino acid sequences encoding a natriuretic compound;

(b) optionally comprising a spacer sequence between each set or adjacent natriuretic compound encoding sequences;

(c) optionally comprising an extension at either or both ends of the multipeptide, the extension comprising one or more amino acids.

27. (Previously presented) The natriuretic compound conjugate of claim 26 wherein the natriuretic peptide units each comprise hBNP (SEQ ID NO. 73) or a biologically active analog, segment or segment analog thereof.

28. (Original) The natriuretic compound conjugate of claim 1 wherein the natriuretic compound consists of a native BNP.

29. (Original) The natriuretic compound conjugate of claim 1 wherein the natriuretic compound consists of a native hBNP.

30. (Original) The natriuretic compound conjugate of claim 1 wherein the natriuretic compound consists of a native ANP.

31. (Original) The natriuretic compound conjugate of claim 1 wherein the natriuretic compound consists of a canine BNP.

32. (Original) The natriuretic compound conjugate of claim 1 wherein the natriuretic compound consists of urodilatin.

33. (Original) The natriuretic compound conjugate of claim 1 wherein the natriuretic compound consists of DNP.

34. (Previously presented) The natriuretic compound conjugate of claim 1 wherein the natriuretic compound comprises an amino acid sequence:

X^1MVQGSGCFGRX^2MDRISSSSGLGCX^3 (SEQ ID NO. 126),

wherein X^1, X^2 and X^3 are each independently selected from the group consisting of Lys, Gly and Arg, with the proviso that at least one of X^1, X^2 and X^3 is Arg or Gly.

35. (Previously presented) The natriuretic compound conjugate of claim 34 wherein the sequence comprises:

(a) N-terminal to X^1, an extension selected from the group consisting of: SPK, PK and K; and/or

(b) C-terminal to X^3, an extension selected from the group consisting of -VLRRH (SEQ ID NO: 19), -VLRR (SEQ ID NO: 20), -VLR, -VL, and -V.

36. (Original) The natriuretic compound conjugate of claim 34 wherein X^1 is Lys, X^2 is Arg and X^3 is Arg.

37. (Previously presented) The natriuretic compound conjugate of claim 1 wherein the natriuretic compound comprises an amino acid sequence:

CFGRX^{1}MDRISSSSGLGCX^2 (SEQ ID NO: 21),

wherein X^1 and/or X^2 comprises a modifying moiety conjugation site coupled to the modifying moiety.

38. (Original) The natriuretic compound conjugate of claim 37 wherein X^1 comprises Lys coupled to the modifying moiety.

39. (Original) The natriuretic compound conjugate of claim 37 wherein X^2 comprises Lys coupled to the modifying moiety.

40. (Original) The natriuretic compound conjugate of claim 1 wherein the modifying moiety conjugation site comprises a moiety selected from the group consisting of natural or non-natural amino acid side chains, an N-terminus of the natriuretic compound, and a C-terminus of the natriuretic compound.

41. (Original) The natriuretic compound conjugate of claim 40 wherein the modifying moiety conjugation site is a Lys side chain.

42. (Original) The natriuretic compound conjugate of claim 1 wherein the natriuretic compound conjugate includes only one modifying moiety.

43. (Currently amended) The natriuretic compound conjugate of claim 1 wherein:

(a) the natriuretic compound comprises a Lys^3 to Cys^{26} segment of hBNP (SEQ ID NO. 127) and a disulfide bond coupling Cys^{10} of the segment to the Cys^{26};

a single modifying moiety coupled to the natriuretic compound at the Lys^3, <u>wherein the amino acid sequence of hBNP is SEQ ID NO. 73.</u>

44. (Previously presented) The natriuretic compound conjugate of claim 1 wherein the natriuretic compound comprises a Cys^{10} to Cys^{26} segment of hBNP (SEQ ID NO. 128) and a disulfide bond coupling the Cys^{10} to the Cys^{26}, wherein said natriuretic compound is a monoconjugate including a single modifying moiety coupled thereto at Lys^{14} of the segment.

45. (Previously presented) The natriuretic compound conjugate of claim 1 wherein the natriuretic compound comprises a Cys^{10} to Lys^{27} segment of hBNP (SEQ ID NO. 129), wherein said natriuretic compound is a monoconjugate including a single modifying moiety coupled thereto at Lys^{27} of the segment.

46. (Original) The natriuretic compound conjugate of claim 1 wherein the natriuretic compound comprises a Cys^{10} to His^{32} (SEQ ID NO. 130) segment of hBNP and a disulfide bond coupling the Cys^{10} to Cys^{26} of the segment, wherein said natriuretic compound is a monoconjugate including a single modifying moiety coupled thereto at Lys^{27} of the segment.

47. (Original) The natriuretic compound conjugate of claim 1 wherein the natriuretic compound comprises a Cys^{10} to Cys^{26} segment of hBNP (SEQ ID NO. 128) and a disulfide bond coupling the Cys^{10} to the Cys^{26}; wherein the natriuretic compound is a monoconjugate including a single modifying moiety coupled thereto at the N-terminus of the natriuretic compound.

48. (Currently amended) The natriuretic compound conjugate of claim 1 wherein:

(a) the natriuretic compound consists of the hBNP amino acid sequence; and

(b) the natriuretic compound conjugate is a diconjugate comprising:

(c) a modifying moiety coupled to the natriuretic peptide at Lys^{3} of the hBNP amino acid sequence, wherein the amino acid sequence of hBNP is SEQ ID NO. 73, and .

(d) a modifying moiety coupled to the natriuretic peptide at Lys^{14} of the hBNP amino acid sequence, wherein the amino acid sequence of hBNP is SEQ ID NO. 73.

49. (Original) The natriuretic compound conjugate of claim 1 wherein:

(a) the natriuretic compound is hBN, wherein the amino acid sequence of hBNP is SEQ ID NO. 73; and

(b) the natriuretic compound conjugate is a diconjugate comprising:

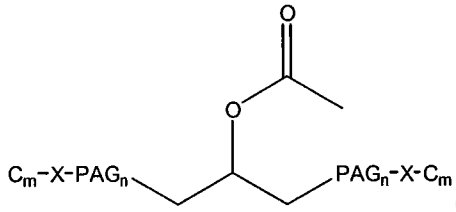
(i) a modifying moiety coupled to the natriuretic peptide at Lys^3 of the hBNP amino acid sequence; and

(ii) a modifying moiety coupled to the natriuretic peptide at Lys^{27} of the hBNP amino acid sequence.

50. (Original) The natriuretic compound conjugate of claim 1 wherein the natriuretic compound sequence comprises an N-terminal tail and the modifying moiety is coupled to an amino acid which is positioned in the N-terminal tail.

51. (Original) The natriuretic compound conjugate of claim 50 wherein the N-terminal tail consists of a native sequence of an N-terminal tail of a natriuretic peptide or a C-terminal segment of an N-terminal tail of a natriuretic peptide.

52. (Original) The natriuretic compound conjugate of claim 1 wherein the modifying moiety has a formula:



(Formula I)

wherein

each C is independently selected and is an alkyl moiety having m carbons and m is from 1 to 20; and

each PAG is independently selected and is a polyalkylene glycol moiety having n subunits and n is from 2 to 25;

each X is independently selected and is a linking moiety.

53. (Original) The natriuretic compound conjugate of claim 52 wherein m is from 1 to 18.

54. (Original) The natriuretic compound conjugate of claim 52 wherein m is from 1 to 16.

55. (Original) The natriuretic compound conjugate of claim 52 wherein n is from 2 to 20.

56. (Original) The natriuretic compound conjugate of claim 52 wherein n is from 2 to 15.

57. (Original) The natriuretic compound conjugate of claim 52 wherein n is from 2 to 10.

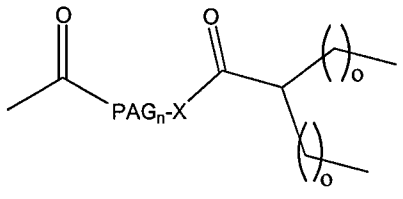
58. (Original) The natriuretic compound conjugate of claim 52 wherein each X is independently selected from the group consisting of -C-, -O-, -C(O)-, -NH-, -NHC(O)-, and -C(O)NH-.

59. (Original) The natriuretic compound conjugate of claim 52 wherein the modifying moiety renders the natriuretic compound more lipophilic than a corresponding unconjugated natriuretic compound.

60. (Original) The natriuretic compound conjugate of claim 52 wherein the modifying moiety renders the natriuretic compound more hydrophilic than a corresponding unconjugated natriuretic compound.

61. (Original) The natriuretic compound conjugate of claim 52 wherein the modifying moiety renders the natriuretic compound more amphiphilic than a corresponding unconjugated natriuretic compound.

62. (Original) The natriuretic compound conjugate of claim 1 wherein the modifying moiety has a formula:



(Formula II)

PAG is a polyalkylene glycol moiety having n subunits and n is from 2 to 25;

X is O or N; and

each o is independently selected and is from 1 to 15.

63. (Original) The natriuretic compound conjugate of claim 62 wherein n is from 2 to 20.

64. (Original) The natriuretic compound conjugate of claim 62 wherein n is from 2 to 15.

65. (Original) The natriuretic compound conjugate of claim 62 wherein n is from 2 to 10.

66. (Original) The natriuretic compound conjugate of claim 62 wherein each o is independently selected and is from 1 to 13.

67. (Original) The natriuretic compound conjugate of claim 62 wherein each o is independently selected and is from 1 to 9.

68. (Original) The natriuretic compound conjugate of claim 62 wherein each o is independently selected and is from 1 to 6.

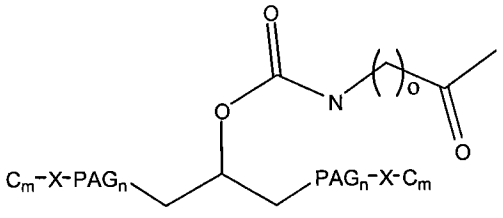
69. (Original) The natriuretic compound conjugate of claim 62 wherein each X is -O-.

70. (Original) The natriuretic compound conjugate of claim 62 wherein the modifying moiety renders the natriuretic compound more lipophilic than a corresponding unconjugated natriuretic compound.

71. (Original) The natriuretic compound conjugate of claim 62 wherein the modifying moiety renders the natriuretic compound more hydrophilic than a corresponding unconjugated natriuretic compound.

72. (Original) The natriuretic compound conjugate of claim 62 wherein the modifying moiety renders the natriuretic compound more amphiphilic than a corresponding unconjugated natriuretic compound.

73. (Original) The natriuretic compound conjugate of claim 1 wherein the modifying moiety has a formula:



(Formula III)

each C is independently selected and is an alkyl moiety having m carbons and m is from 1 to 20; and

each PAG is independently selected and is a polyalkylene glycol moiety having n subunits and n is from 2 to 25;

each X is independently selected and is a linking moiety.

o is from 1 to 15.

74. (Original) The natriuretic compound conjugate of claim 73 wherein m is from 1 to 18.

75. (Original) The natriuretic compound conjugate of claim 73 wherein m is from 1 to 16.

76. (Original) The natriuretic compound conjugate of claim 73 wherein n is from 2 to 20.

77. (Original) The natriuretic compound conjugate of claim 73 wherein n is from 2 to 15.

78. (Original) The natriuretic compound conjugate of claim 73 wherein n is from 2 to 10.

79. (Original) The natriuretic compound conjugate of claim 73 wherein o is from 1 to 13.

80. (Original) The natriuretic compound conjugate of claim 73 wherein o is from 1 to 9.

81. (Original) The natriuretic compound conjugate of claim 73 wherein o is from 1 to 6.

82. (Original) The natriuretic compound conjugate of claim 73 wherein each X is independently selected from the group consisting of -C-, -O-, -C(O)-, -NH-, -NHC(O)-, and -C(O)NH-.

83. (Original) The natriuretic compound conjugate of claim 73 wherein the modifying moiety renders the natriuretic compound more lipophilic than a corresponding unconjugated natriuretic compound.

84. (Original) The natriuretic compound conjugate of claim 73 wherein the modifying moiety renders the natriuretic compound more hydrophilic than a corresponding unconjugated natriuretic compound.

85. (Original) The natriuretic compound conjugate of claim 73 wherein the modifying moiety renders the natriuretic compound more amphiphilic than a corresponding unconjugated natriuretic compound.

86. (Original) The natriuretic compound conjugate of claim 1 wherein the modifying moiety comprises a linear or branched polyalkylene glycol moiety.

87. (Original) The natriuretic compound conjugate of claim 1 wherein the modifying moiety comprises a sugar moiety coupled to an alkyl moiety.

88. (Original) The natriuretic conjugate of claim 87 wherein the modifying moiety further comprises a sugar moiety.

89. (Original) The natriuretic compound conjugate of claim 86 wherein the polyalkylene glycol moiety comprises a polyethylene glycol moiety.

90. (Original) The natriuretic compound conjugate of claim 86 wherein the polyalkylene glycol moiety has from 2 to 25 polyalkylene glycol subunits.

91. (Original) The natriuretic compound conjugate of claim 86 wherein the polyalkylene glycol moiety has from 2 to 20 polyalkylene glycol subunits.

92. (Original) The natriuretic compound conjugate of claim 86 wherein the polyalkylene glycol moiety has from 2 to 15 polyalkylene glycol subunits.

93. (Original) The natriuretic compound conjugate of claim 86 wherein the polyalkylene glycol moiety has from 2 to 10 polyalkylene glycol subunits.

94. (Original) The natriuretic compound conjugate of claim 86 wherein the modifying moiety further comprises a linear or branched alkyl moiety.

95. (Original) The natriuretic compound conjugate of claim 94 wherein the modifying moiety further comprises a sugar moiety.

96. (Original) The natriuretic compound conjugate of claim 94 wherein the alkyl moiety has from 1 to 20 carbons.

97. (Original) The natriuretic compound conjugate of claim 94 wherein the alkyl moiety has from 1 to 18 carbons.

98. (Original) The natriuretic compound conjugate of claim 94 wherein the alkyl moiety has from 1 to 16 carbons.

99. (Original) The natriuretic compound conjugate of claim 94 wherein the alkyl moiety is separated from the polyalkylene glycol moiety by a linker selected from the group consisting of -C-, -O-, -C(O)-, -NH-, -NHC(O)-, and -C(O)NH-.

100. (Original) The natriuretic compound conjugate of claim 94 wherein the modifying moiety renders the natriuretic compound conjugate more lipophilic than a corresponding unconjugated natriuretic compound.

101. (Original) The natriuretic compound conjugate of claim 94 wherein the modifying moiety comprises a bond coupling the polyalkalene glycol moiety to the alkyl moiety which bond is hydrolysable *in vivo*.

102. (Original) The natriuretic compound conjugate of claim 1 wherein the modifying moiety comprises a linear or branched polyalkylene glycol moiety coupled to the natriuretic compound and a linear or branched alkyl moiety coupled to the polyalkalene glycol moiety at a site which is distal relative to the natriuretic compound.

103. (Original) The natriuretic compound conjugate of claim 1 wherein the modifying moiety comprises a linear or branched alkyl moiety coupled to the natriuretic compound and a polyalkylene glycol moiety coupled to the alkyl moiety at a site which is distal relative to the natriuretic compound.

104. (Original) The natriuretic compound conjugate of claim 1 wherein the modifying moiety is selected from the group consisting of the oligomeric moieties of **Table 1**.

105. (Original) The natriuretic compound conjugate of claim 1 wherein the modifying moiety is coupled to the natriuretic compound by a bond that is hydrolysable *in vivo*.

106. (Original) The natriuretic compound conjugate of claim 1 wherein the modifying moiety is coupled to the natriuretic compound by a bond that is hydrolysable in the bloodstream.

107. (Original) The natriuretic compound conjugate of claim 1 wherein the modifying moiety is coupled to the natriuretic compound by a bond that is not hydrolysable *in vivo*.

108. (Original) The natriuretic compound conjugate of claim 1 wherein the modifying moiety is coupled to the natriuretic compound by a bond that is not hydrolysable in the bloodstream.

109. (Original) The natriuretic compound conjugate of claim 1 wherein the modifying moiety is coupled to the natriuretic compound by a bond selected from the group consisting of ester, carbonate, carbamate, amide, ether, and amine.

110. (Original) The natriuretic compound conjugate of claim 1 wherein the modifying moiety is hydrolysable *in vivo* to yield a pegylated natriuretic compound.

111. (Original) The natriuretic compound conjugate of claim 110 wherein the modifying moiety is hydrolysable *in vivo* to yield a pegylated natriuretic compound comprising one or more PEG moieties having from 1 to 6 PEG units.

112. (Original) A pharmaceutical formulation comprising the natriuretic compound conjugate of claim 1.

113. (Original) The pharmaceutical formulation of claim 112 formulated for a route of delivery selected from the group consisting of enteral, perenteral, oral, subcutaneous, sublingual, buccal, nasal, intravenous and intramuscular.

114. (Original) A method of treating a condition characterized by an excessive level of extracellular fluid, the method comprising administering to a subject in need thereof a pharmaceutically acceptable amount of a natriuretic compound conjugate of claim 1.

115. (Original) The method of claim 114 wherein the condition comprises congestive heart failure.

116. (Original) The method of claim 114 wherein the condition comprises chronic congestive heart failure.

117. (Original) The method of claim 114 wherein the condition comprises acute congestive heart failure.

118. (Original) The method of claim 114 wherein the natriuretic compound conjugate is self-administered.

119. (Original) The method of claim 114 wherein the natriuretic compound conjugate is orally administered.

120. (Original) The method of claim 114 wherein the natriuretic compound conjugate is administered via a route of administration selected from the group consisting of enteral, perenteral, oral, subcutaneous, sublingual, buccal, nasal, intravenous and intramuscular.

121. (Original) The method of claim 114 wherein the condition is hypertension.

122. (Original) A method of making the natriuretic compound conjugate of claim 1, the method comprising:

(a) conjugating a natriuretic peptide multipeptide comprising two or more natriuretic compound units;

(b) cleaving the natriuretic peptide multipeptide to yield natriuretic compound conjugate;

(c) oxidizing the cleaved natriuretic compound conjugate to form one or more disulfide bonds in the natriuretic compound conjugate.

123. (Previously presented) The method of claim 122 wherein the natriuretic compound comprises Cys^{10} to Cys^{26} of hBNP (SEQ ID NO. 128) and step 122(c) yields a disulfide bond between the Cys^{10} and Cys^{26}.

124. (Original) A method of making the natriuretic compound conjugate of claim 1, the method comprising:

(a) making a multi-peptide natriuretic compound comprising two or more natriuretic compound units;

(b) cleaving the natriuretic peptide multipeptide to yield natriuretic peptide compound;

(c) conjugating the natriuretic compound to yield natriuretic compound conjugate;

(d) oxidizing the cleaved natriuretic compound conjugate to form one or more disulfide bonds in the natriuretic compound conjugate.

125. (Previously presented) The method of claim 124 wherein the natriuretic compound comprises Cys^{10} to Cys^{26} of hBNP (SEQ ID NO. 128) and step 122(c) yields a disulfide bond between the Cys^{10} and Cys^{26}.

126. (Original) A method of making the natriuretic compound conjugate of claim 1, the method comprising:

(a) making a multi-peptide natriuretic compound comprising two or more natriuretic compound units;

(b) cleaving the natriuretic peptide multipeptide to yield natriuretic compound;

(c) oxidizing the cleaved natriuretic compound to form one or more disulfide bonds in the natriuretic compound; and

(d) conjugating the natriuretic compound.

127. (Original) A modified pro-polynatriuretic peptide conjugate comprising:

(a) at least one natureteic peptide unit having a modifying moiety conjugation site and an NPR-A binding site;

(b) at least one modifying moeity attached to the modifying moiety conjugation site of at least one of the natriuretic peptide units;

(c) a leader sequence; and

(d) an enzymatically cleavable spacer coupling the leader sequence to a first natriuretic peptide conjugate.

128. (Original) A natriuretic peptide analog comprising an amino acid sequence having at least one modifying moiety conjugation site, an NPR-A binding region and at least one substituted Lys residue therein as compared to a native natriuretic peptide amino acid sequence, wherein said substituted Lys residue is not the amino acid modifying moiety conjugation site.

129. (Currently amended) The natriuretic peptide analog of claim 128, wherein the native natriuretic peptide has the amino acid sequence SEQ ID NO. 73, wherein the one or more substituted Lys residues comprise a substitution selected from the group consisting of: Lys3Gly, Lys3Arg, Lys14Gly, Lys14Arg, Lys27Gly, or Lys27Arg.

130. (Previously presented) The natriuretic peptide analog of claim 128 comprising a structure:

SPKMVQGSGCFGRX^{1}MDRISSSSGLGCX^{2}VLRRH (SEQ ID NO: 131)

wherein X^1 is Lys and X^2 is other than Lys, or X^1 is Lys and X^2 is other than Lys, or X^1 and X^2 are other than Lys.

131. (Original) The natriuretic peptide analog of claim 130 wherein X^1 is Lys and X^2 is Arg or Gly, or X^1 is Lys and X^2 is Arg or Gly, or X^1 and X^2 are independently selected and are Arg or Gly.

132. (Previously presented) A natriuretic peptide analog comprising a structure:

CFGRX^{1}MDRISSSSGX^{2}GC (SEQ ID NO: 132)

wherein X^1 is an amino acid that does not comprise a conjugation site, and X^2 is an amino acid that comprises a modifying moiety conjugation site.

133. (Original) The natriuretic peptide analog of claim 132 wherein X^1 is Arg and X^2 is Lys.

134. (Previously presented) A natriuretic peptide analog having a structure:

X^1-CFGRX^{3}MDRISSSSGLGC-X^2 (SEQ ID No. 117)

wherein X^1 is an amino acid sequence having from 1 to 10 amino acids, X^2 is an amino acid sequence having from 1 to 10 amino acids, and X^3 is other than Lys.

135. (Original) The natriuretic peptide analog of claim 134 wherein X^3 is Arg or Gly.

136. (Previously presented) The natriuretic peptide analog of claim 134 wherein X^1 is SPY^{1}MVQGSG (SEQ ID NO: 133), wherein Y^1 comprises a modifying moiety conjugation site.

137. (Original) The natriuretic peptide analog of claim 134 wherein X^1 is selected from the group consisting of:

(a) N-terminal tails and C-terminal segments of N-terminal tails of natriuretic peptides;

(b) N-terminal tails and C-terminal segments of (a) comprising a substitution selected from the group consisting of Lys-to-Gly and Lys-to-Arg;

(c) N-terminal tails and C-terminal segments of (a) comprising a substitution selected from the group consisting of Gly-to-Lys and Arg-to-Lys;

(d) N-terminal tails and C-terminal segments of (a) comprising an inserted Lys.

138. (Previously presented) The natriuretic peptide analog of claim 134 wherein X^2 is Y^2VLRRH (SEQ. ID. NO: 134), wherein Y^2 is other than Lys.

139. (Original) The natriuretic peptide analog of claim 138 wherein Y^2 is Arg.

140. (Original) The natriuretic peptide analog of claim 134 wherein X^2 is selected from the group consisting of:

(a) C-terminal tails and N-terminal segments of C-terminal tails of natriuretic peptides;

(b) C-terminal tails and N-terminal segments of C-terminal tails of 137(a) comprising a substitution selected from the group consisting of Lys-to-Gly and Lys-to-Arg;

(c) C-terminal tails and N-terminal segments of C-terminal tails of 137(a) comprising a substitution selected from the group consisting of Gly-to-Lys and Arg-to-Lys;

(d) C-terminal tails and N-terminal segments of C-terminal tails of 137(a) comprising an inserted Lys.

141. (Previously presented) A natriuretic peptide analog having a structure:

X^1-CFGRX^3MDRIGLGC-X^2 (SEQ ID No. 135)

wherein X^1 is a peptide of from 1 to 9 amino acids, X^2 is a peptide of from 1 to 6 amino acids, and X^3 is other than Lys.

142. (Original) The natriuretic peptide analog of claim 140 wherein X^3 is Arg or Gly.

143. (Previously presented) The natriuretic peptide analog of claim 142 wherein X^1 is SPY^1MVQGSG (SEQ ID NO: 133), wherein Y^1 comprises a modifying moiety conjugation site.

144. (Previously presented) The natriuretic peptide analog of claim 142 wherein X^2 is Y^2VLRRH (SEQ. ID. NO: 134), wherein Y^2 is other than Lys.

145. (Original) The natriuretic peptide analog of claim 144 wherein Y^2 is Arg.

146. (Previously presented) The natriuretic peptide analog of claim 144 wherein X^3 is Arg, X^1 is a sequence SPKMVQGSG (SEQ ID NO: 122) and X^2 is a sequence RVL.

147. (Previously presented) A natriuretic peptide analog having a structure X^1-CFGRX^3MDRIX^4GLGC-X^2 (SEQ ID NO. 136) wherein

(a) X^1 is an amino acid sequence of from 1 to 10 amino acids,

(b) X^2 is an amino acid sequence of from 1 to 10 amino acids,

(c) X^4 is an amino acid sequence of from 1 to 4 amino acids; and

(d) X^3 is other than Lys.

148. (Original) The natriuretic peptide analog of claim 147 wherein neither X^1 nor X^2 is a sequence native to a natriuretic peptide.

149. (Original) The natriuretic peptide of claim 147 where X^3 is Arg or Gly.

150. (Previously presented) The natriuretic peptide of claim 147 where X^1 is SPY^1MVQGSG (SEQ ID NO: 133) wherein Y^1 comprises a modifying moiety conjugation site.

151. (Previously presented) The natriuretic peptide analog of claim 147 wherein X^2 is Y^2VLRRH (SEQ. ID. NO: 134), wherein Y^2 is other than Lys.

152. (Original) The natriuretic peptide analog of claim 151 wherein Y^2 is Arg.

153. (Currently amended) An hBNP analog comprising a substitution of Lys14Arg or Lys14Gly, wherein the amino acid sequence of hBNP is SEQ ID NO. 73.

154. (Currently amended) An hBNP analog comprising a substitution of Lys27Arg or Lys27Gly, wherein the amino acid sequence of hBNP is SEQ ID NO. 73.

155. (Currently amended) An hBNP analog comprising a substitution of Lys3Arg or Lys3Gly, wherein the amino acid sequence of hBNP is SEQ ID NO. 73.

156. (Original) A natriuretic compound conjugate comprising:

(a) a natriuretic compound comprising:

(i) a natriuretic molecule NPR-A binding site; and

(ii) at least one modifying moiety conjugation site; and

(b) at least one modifying moiety attached to said modifying moiety conjugation site;

wherein said natriuretic compound retains a therapeutically significant percentage of cGMP stimulating activity relative to a corresponding unconjugated natriuretic compound.

157. (Original) A natriuretic compound conjugate comprising:

(a) a natriuretic compound comprising:

(i) a natriuretic molecule NPR-A binding site; and

(ii) at least one modifying moiety conjugation site; and

(b) at least one modifying moiety attached to said modifying moiety conjugation site;

wherein said natriuretic compound conjugate retains at least 50% of the cGMP stimulating activity of a corresponding unconjugated natriuretic compound.

158. (Original) A natriuretic compound conjugate comprising:

(a) a natriuretic compound comprising:

(i) a natriuretic molecule NPR-A binding site; and

(ii) at least one modifying moiety conjugation site; and

(b) at least one modifying moiety attached to said modifying moiety conjugation site;

wherein said natriuretic compound conjugate is more hydrophilic than a corresponding unconjugated natriuretic compound.

159. (Original) A natriuretic compound conjugate comprising:

(a) a natriuretic compound comprising:

(i) a natriuretic molecule NPR-A binding site; and

(ii) at least one modifying moiety conjugation site; and

(b) at least one modifying moiety attached to said modifying moiety conjugation site;

wherein said natriuretic compound conjugate is more amphiphilic than a corresponding unconjugated natriuretic compound.

160. (Original) A natriuretic compound conjugate comprising:

(a) a natriuretic compound comprising:

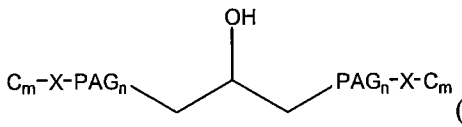
(i) a natriuretic molecule NPR-A binding site; and

(ii) at least one modifying moiety conjugation site; and

(b) at least one modifying moiety attached to said modifying moiety conjugation site;

wherein the natriuretic compound conjugate is more lipophilic than a corresponding unconjugated natriuretic compound, wherein at least one modifying moiety does not consist of an alkyl moiety.

161. (Original) A compound having a formula:



(Formula IV)

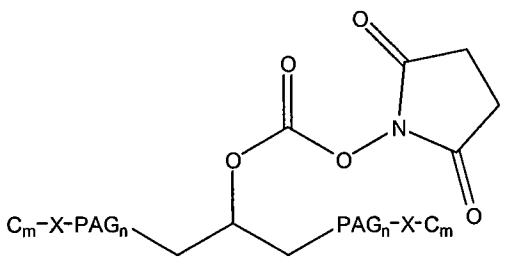
wherein

each C is independently selected and is an alkyl moiety having m carbons and m is from 1 to 20; and

each PAG is independently selected and is a polyalkylene glycol moiety having n subunits and n is from 2 to 25;

each X is independently selected and is a linking moiety.

162. (Original) A compound having a formula:



(Formula V)

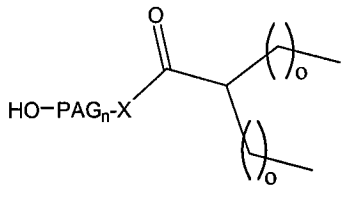
wherein

each C is independently selected and is an alkyl moiety having m carbons and m is from 1 to 20; and

each PAG is independently selected and is a polyalkylene glycol moiety having n subunits and n is from 2 to 25;

each X is independently selected and is a linking moiety.

163. (Original) A compound having a formula:



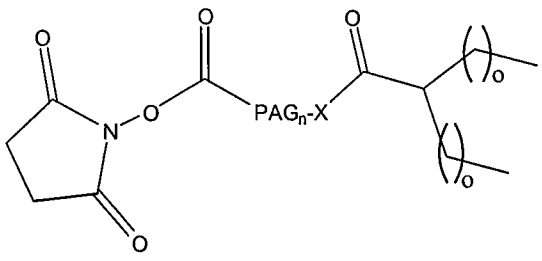
(Formula VI)

PAG is a polyalkylene glycol moiety having n subunits and n is from 2 to 25;

X is O or N; and

each o is independently selected and is from 1 to 15.

164. (Original) A compound having a formula:



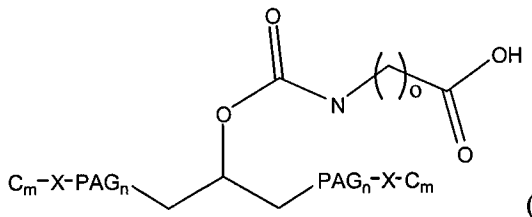
(Formula VII)

PAG is a polyalkylene glycol moiety having n subunits and n is from 2 to 25;

X is O or N; and

each o is independently selected and is from 1 to 15.

165. (Original) A compound having a formula:



(Formula VIII)

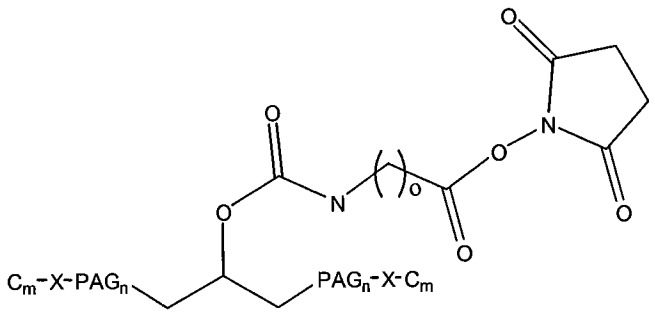
each C is independently selected and is an alkyl moiety having m carbons and m is from 1 to 20; and

each PAG is independently selected and is a polyalkylene glycol moiety having n subunits and n is from 2 to 25;

each X is independently selected and is a linking moiety.

o is from 1 to 15.

166. (Original) A compound having a formula:



(Formula IX)

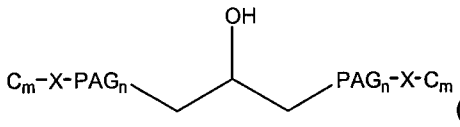
each C is independently selected and is an alkyl moiety having m carbons and m is from 1 to 20; and

each PAG is independently selected and is a polyalkylene glycol moiety having n subunits and n is from 2 to 25;

each X is independently selected and is a linking moiety;

o is from 1 to 15.

167. (Original) A method of making a compound of the formula:



(Formula IV)

wherein

each C is independently selected and is an alkyl moiety having m carbons and m is from 1 to 20; and

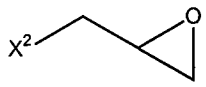
each PAG is independently selected and is a polyalkylene glycol moiety having n subunits and n is from 2 to 25;

each X is independently selected and is a linking moiety;

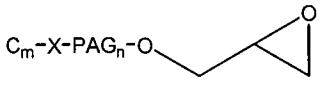
the method comprising:

(a) reacting a compound of formula:

with a compound of formula:



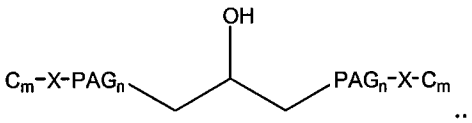
where X^2 is a halide, and wherein the reaction is carried out in the presence of a base and a solvent to yield:



; and

(b) reacting the product of (a) with a compound of formula:

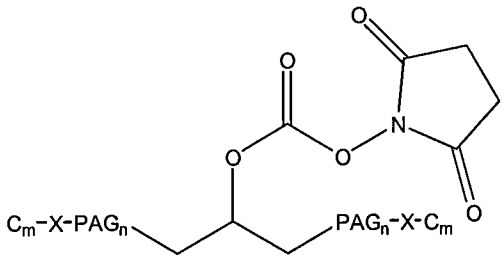
in the presense of a Lewis acid and a solvent to yield:



168. (Original) The method of claim 167 wherein the base is NaH and the solvent is tetrahydrofuran.

169. (Original) The method of claim 167 wherein the Lewis acid is BF_3OEt_2.

170. (Previously presented) A method of making a compound of the formula:



(Formula V)

wherein

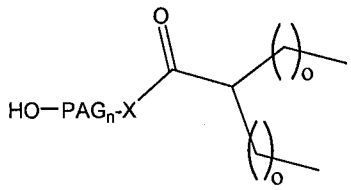
each C is independently selected and is an alkyl moiety having m carbons and m is from 1 to 20; and

each PAG is independently selected and is a polyalkylene glycol moiety having n subunits and n is from 2 to 25;

each X is independently selected and is a linking moiety;

the method comprising reacting the product of claim 161 with paranitrochloroformate or disuccimidyl carbonate.

171. (Original) A method of making a compound of the formula:



wherein

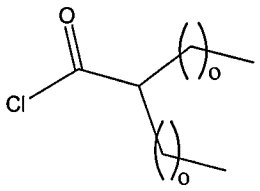
PAG is a polyalkylene glycol moiety having n subunits and n is from 2 to 25;

X is O or N; and

each o is independently selected and is from 1 to 15;

the method comprising:

reacting a compound of formula:

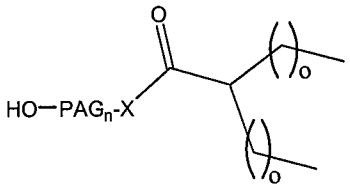


wherein o is as defined above, with a compound of formula:

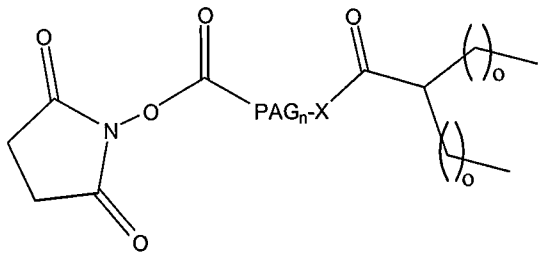
$$HO{-}PAG_n\text{-}X$$

where X is –NH or –OH;

in solvent, to yield a compound of formula:



172. (Original) A method of making a compound of the formula:



(Formula VII)

wherein

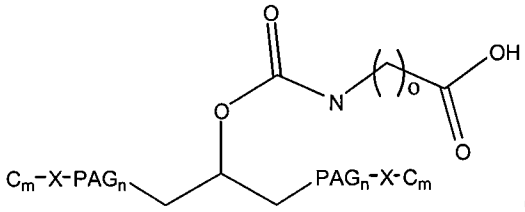
PAG is a polyalkylene glycol moiety having n subunits and n is from 2 to 25;

X is O or N; and

each o is independently selected and is from 1 to 15;

the method comprising activating a product of claim 170 using an activating agent selected from the group consisting of disuccinimidyl carbonate, paranitrochloroformate, phosgene and N-hydroxysuccinimide.

173. (Previously presented) A method of making a compound of the formula:



(Formula VIII)

wherein

each C is independently selected and is an alkyl moiety having m carbons and m is from 1 to 20; and

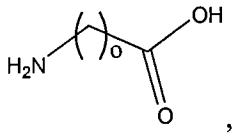
each PAG is independently selected and is a polyalkylene glycol moiety having n subunits and n is from 2 to 25;

each X is independently selected and is a linking moiety.

o is from 1 to 15;

the method comprising:

reacting the product of claim 161 with a compound of formula:

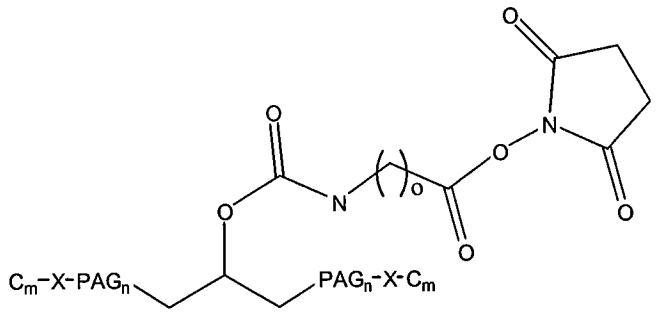


,

in the presence of a base in a solvent.

174. (Original) The method of claim 173 wherein the base is K_2CO_3 and the solvent is an aqueous and/or organic solvent.

175. (Previously presented) A method of making a compound of the formula:



(Formula IX)

wherein

each C is independently selected and is an alkyl moiety having m carbons and m is from 1 to 20; and

each PAG is independently selected and is a polyalkylene glycol moiety having n subunits and n is from 2 to 25;

each X is independently selected and is a linking moiety;

o is from 1 to 15;

the method comprising reacting a compound produced according to the method of claim 173 with N-hydroxysuccinimide.

176. (Previously presented) A natriuretic peptide analog comprising a structure:

SP**X**^{1}MMH**X**^{2}SGCFGRRLDRIGSLSGLGCNVLR**X**^{3}Y (SEQ ID NO. 137)

wherein X^1 is Lys, Arg or His, X^2 is Lys, Arg, His, and X^3 is Arg or His.

177. (Original) The natriuretic peptide analog of claim 176 comprising a modifying moiety conjugated at the S residue.

178. (Previously presented) A natriuretic peptide analog comprising a structure:

SP**Z**^{1}MVQGSG-CFGR**Z**^{2}MDRISSSS**X**^{1}**X**^{2}**X**^{3}C (SEQ ID NO. 113)

wherein Z^1 is Arg or an amino acid other than Lys, and wherein Z^2 is Arg or an amino acid other than Lys, wherein X^1 is Gly, Met, Leu, Phe, Ile or a conservative substitution thereof, wherein X^2 is Leu, Trp, Tyr, Phe or a conservative substitution thereof, and wherein X^3 is Gly and Arg, or a conservative substitution thereof.

179. (Original) The natriuretic peptide analog of claim 178 where Z^1 is Lys and Z^2 is other than Lys.

180. (Previously presented) A natriuretic peptide analog comprising a structure:

K CFKGKNDR**X**^{1} K**X**^{2} QSGL**X**^{3} C-NSFKY (SEQ ID NO. 114)

wherein X^1 is T, a, R, H, P, T, E;

wherein X^2 is K, N-methyl, Arg, S, D,P;

wherein X^3 is Arg, K, Y, F, S, P, Orn, Har, Har, p-amidinophenyl Ala, I, any other amino acid that has a positive charge other than Gly, or Try.

181. (Original) The natriuretic peptide of claim 178 or 180 further defined as comprising a natriuretic peptide conjugate, comprising a modifying moiety conjugated to one or more of the Lys residues therein.

REMARKS

According to the November 16, 2006 Notice to comply, the Office of Initial Patent Examination found some of the claims lacking a necessary sequence identifier. Applicants have amended the necessary claims.

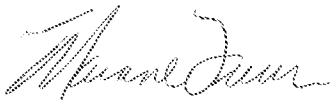
Applicants insists that the previously submitted sequence listing and computer readable disk are acceptable because there was no fault found with the submitted sequence material. The mere addition of sequence identifiers to claims does not warrant the submission of duplicate copies of sequence listings and/or disk containing same, especially when the previous submission has already met all the requirements.

Fees Payable/Petition for Extension

Applicants request a two month extension for responding to the November 16, 2006 Notice thereby extending the due date from December 16, 2006 to February 16, 2007. The extension fee for a large entity is $450.00. Please charge such fee and any addition fee required for entry of the amendment to Deposit Account No. 13-4365 of Moore & Van Allen.

If any issues remain please contact the undersigned attorney at 919-286.8089.

Respectfully submitted



Marianne Fuierer
Attorney for Applicants
Registration No. 39983